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SANTA BARBARA • SANTA CRUZ

SCHOOL OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94143

October 19, 1977

Dr. John Z. Bowers
Josiah Macy, Jr. Foundation
One Rockefeller Plaza
New York, New York 10020

Dear Dr. Bowers:

Thank you for your letter of October 13. Frankly, it was my first news of Michael Stoker's new job, and I have written to him, asking for the confirmation you requested.

As I explained in the preamble to my peculiar research plan, my activities were likely to be determined in part by circumstances. Since I wrote the plan, the writing on the wall seems clearer. I have had considerable difficulty obtaining the necessary reagents for the hepatitis work, and my realistic assessment is that little or no work will be done on this project until I return to San Francisco in mid-1979. Secondly, I have been corresponding with Mike Fried at ICRF about the feasibility of initiating the molecular cloning experiments in London. The bureaucratic obstacles appear large and cannot be overcome from this distance. For the moment, my plan is to ask after I arrive for permission to do one experiment---cloning of mouse mammary tumor virus integration sites from mouse cells, using a polyoma vector. This experiment has many virtues from a biological point of view, and the additional virtue of utilizing Mike Fried's expertise with the polyoma system. The rest of the cloning plans will presumably await NIH certification of the newly-recommended guidelines for recombinant DNA research; these new guidelines would allow us to proceed with most or all of the proposed cloning experiments, using plasmid vectors, in our local P3 facilities. As a result of the above difficulties, I am planning to pursue most actively the plans to generate deletion mutants of avian leukosis viruses. This project has the advantage of integrating me most fully into life at ICRF (both with Mike Fried as advisor in making deletion mutants and with the RNA tumor virologists as consultants about the biology of leukosis viruses). Moreover, I think the feasibility of these studies is very clear, and their potential applicability to several aspects of my research program very appealing.

I hope this explanation helps to clear the muddy waters.

Yours truly,

A handwritten signature in dark ink, appearing to read "Harold Varmus", is written over a horizontal line.

Harold E. Varmus, M.D.
Associate Professor
Department of Microbiology

HEV/es